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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,939	12/20/2000	Cesare Galli	P66004USO	8697

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	09/647,939	GALLI ET AL.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-21 and 26-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-21 and 26-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's arguments filed September 20, 2006 have been fully considered but they are not persuasive. The amendment has been entered. Claims 19-21 and 26-28 are pending.

The objection to the specification is withdrawn in view of applicant's amendment.

The rejection of claims 19-21 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps is withdrawn in view of applicant's amendments.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-21 stand rejected and new claims 26-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 19-21 and 26-28 are to a method of reconstructing a mammalian embryo comprising reconstructing a first generation embryo comprising transferring a mononuclear cell from the blood or natural secretion of a mammal or a nucleus isolated from a mononuclear cell to an enucleated oocyte, activating the oocyte, developing the embryo to a stage where it can transferred to a uterus, and transferring a cell from the first generation embryo an enucleated oocyte to form a second generation embryo, and a method of reconstructing a mammalian embryo comprising reconstructing a first generation embryo comprising transferring a

mononuclear cell from the blood or natural secretion of a mammal or a nucleus isolated from a mononuclear cells to an enucleated oocyte, preparing fetal fibroblast cultures from the first generation embryo and transferring cells from said fetal fibroblast cultures to an enucleated oocyte suitable recipient to form a second generation embryo, where the fetal fibroblasts are genetically modified, and permitted the development of the embryo to term.

Applicant argues that while Wakayama and Hochedlinger failed to succeed with first generation cloning, Hochedlinger was successful in cloning a mouse using a cell from a first generation mouse embryo. Applicant argues the examiner has not taken into consideration the evidence from Hochedlinger, not has the examiner taken into consideration the successful production of a bovine disclosed in the specification. Applicant argues that second generation cloning leads to the successful production of a live and healthy cloned mammal. Applicant further argues the pipette size and the piezostepper are not essential steps to the claimed invention. Applicant argues the specification only discloses the disruption of the cell membrane to be "optional." These arguments are not persuasive.

Wakayama and Hochedlinger were cited because they address the unpredictability in cloning a mammal by nuclear transfer using a lymphocyte as the donor. The question regarding the ultimate success in Hochedlinger is whether the success was merely due to a second round of nuclear transfer using an embryonic stem cell isolated from a blastocyst resulting from nuclear transfer of a lymphocyte nucleus into an enucleated oocyte, or if the success was due to the formation of tetraploid embryos. See Hochedlinger, page 1035, col. 2, parag. 1, lines 1-4 and parag. 3, lines 1-2. Further, the method of the present specification produced one calf (specification, page 11, Table 1). This is not evidence that the method is reproducible. Further, Further, Wakayama did not achieve blastocysts for transfer

using thymus cells as nuclear donors (Wakayama, page 380, Table 3.). Thus, from the failure Wakayama and the success of Galli, the precise optimization of the size of the pipette and use of a piezostepper is relevant to the claimed invention. A declaration may overcome this part of the rejection if it can be stated the calf disclosed was made without the use of pipette size optimization and use of a piezostepper. From the teachings of Galli, cytoplast membrane rupture is critical to nuclear transfer as claimed (page 168, col. 1, parag. 1, lines 11-17).

Applicant argues it is entirely believable, in view of their positive result, for primates to be produced by the claimed method. Applicant argues complex experimentation does not make an invention undue, or lacking enablement. These arguments are not persuasive.

Mitalipov clearly states somatic cell nuclear transfer was unsuccessful in the production of cloned monkeys (Mitalipov, abstract). Mitalipov further states, clearly, that somatic cell cloning, as is part of the present methods, has not been accomplished in primates (Mitalipov, page 1367, col. 2, parag, 3, lines 1-3). Thus, the art supports the lack of enablement in producing cloned mammals. Simerly offers a reason why primate cloning is unpredictable within the guidance of 35 U.S.C. § 112, first paragraph.

Therefore, at the time of filing, the skilled artisan would have needed to conduct an undue amount of experimentation without a predictable degree of success to implement the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 19 recites the limitation "the uterus" in line 8. There is insufficient antecedent basis for this limitation in the claim. The term "a uterus" should be used.

Claims 19 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19 and 20 at lines 3-5 state "transferring a mononuclear cell or isolated nucleus from the blood or natural secretion of a mammal." This is confusing as to whether a mononuclear cell from the blood or natural secretion or some other cell type. It would be clearer is applicant rewrite the claim as "transferring a mononuclear cell isolated from the blood or natural secretion of a mammal, or the isolated nucleus of said mononuclear cell, or other such language so that it is clear that the cell being isolated from the blood or natural secretion of a mammal is a mononuclear cell.

Claims 19 and 20 are also confusing at line 10 in the phrase "a cell or isolated nucleus from the first generation embryo." The nucleus is isolated from the cell and not the embryo. A suggested rewrite is " a cell isolated from the first generation embryo, or a nucleus isolated from said cell."

Claims 26-28 are improperly dependent on claims 19-21. Each of claims 19-21 is to a method of reconstructing a mammalian embryo. Claims 26-28 depend from these claims and state the embryo develops to term. However, development to term is not a step of reconstructing an embryo. Claims 26-28 should be rewritten a method of producing a mammal, where the reconstructed embryos produced by methods 19-21 are permitted to term development.

The claims are free of the prior art. At the time of filing the prior art did not teach or suggest a method of reconstructing a mammalian embryo comprising

reconstructing a first generation embryo comprising transferring a mononuclear cell from the blood or natural secretion of a mammal to a suitable recipient and transferring a cell from the first generation embryo of a suit a suitable recipient to form a second generation embryo, and a method of reconstructing a mammalian embryo comprising reconstructing a first generation embryo comprising transferring a mononuclear cell from the blood or natural secretion of a mammal to a suitable recipient, preparing fetal fibroblast cultures from the first generation embryo and transferring cells from said fetal fibroblast cultures to a suitable recipient to form a second generation embryo, and where the fetal fibroblasts.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number

is 571-272-0727. The examiner can normally be reached on M-Fri, 7:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

November 30, 2006